

[54] **STABILIZED NITRIC OXIDE - PRIMARY AMINE COMPLEXES USEFUL AS CARDIOVASCULAR AGENTS**

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[56] References Cited

U.S. PATENT DOCUMENTS

2,635,978	4/1953	Massengale	514/499
2,954,314	9/1960	Metzger	514/499
3,153,094	10/1984	Reilly	260/576
3,309,373	3/1967	Danzig	546/6
3,930,970	1/1976	Barton	260/397.5

FOREIGN PATENT DOCUMENTS

62-0175613 4/1987 Japan .

OTHER PUBLICATIONS

Drago & Karstetter, *The Reaction of NO with Various Primary & Secondary Amines*, Aug. 4, 1960, p. 1819, JACS.

Palmer et al., *Nitric Oxide Release Accounts for the Biological Activity of Endothelium-Derived Relaxing Factor*, Nature, pp. 524-526.

CA 108:68610c, *Red Blood Cells Generate Nitric Oxide from Directly Acting, Nitrogenous Vasodilators*, Kruzyna et al.

Palmer et al., Nature, 317, 524-526, 1987.

Kruszyna et al., *Toxicol. and Applied Pharmacol.*, 91, 429-438, 1987.

Ignarro, *The FASEB Journal*, 3, 31-36, 1989.

Ignarro et al., *J. Pharmacol. and Exper. Theraput.*, 218(2), 739-749, 1981.

Atston et al., *The Journal of Biological Chemistry*, 260(7), 4069-4074 and 9948, 1985.

Kubrina et al., *Izvestiia Akademii Nauk SSSR.Seriia Biologicheska* 6, 844-850, 1988 & Abstract.

Drago, "Free Radicals in Inorganic Chemistry", No. 36, *Advances in Chemistry Series*, American Chemical Society, Washington, DC, 1962, pp. 143-149.

Weirsdorff et al., *Chemical Abstracts*, 77: 48034f, 1972.

Fujitsuka et al., *Chemical Abstracts*, 82: 31108p, 1975.

DeLuca et al., *Parenteral Drug Delivery Systems*, pp. 238-250 of "Pharmaceutics and Pharmacy Practice", J. B. Lippincott Co., Philadelphia, 1987.

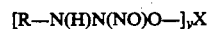
Toissel, ASHP, "Handbook on Injectable Drugs", 4th ed., pp. 622-630, 1986.

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[57] ABSTRACT

A method of treating cardiovascular disorders in a mammal, by administering to said mammal an effective amount of a compound of the formula:



wherein R is loweralkyl, aryl, arylalkyl, or cycloalkyl, any of which R groups may be optionally substituted by one to three substituents selected from the group consisting of: halo, hydroxyl, alkoxy, amino, amido, formyl, carboxyl, or nitro; and wherein X is a pharmaceutically acceptable cation, a pharmaceutically acceptable metal center, or a pharmaceutically acceptable organic group selected from loweralkyl, acyl or amido, and Y is 1 to 3 consistent with the valence of X. Pharmaceutical compositions containing the compounds are also provided.

20 Claims, No Drawings